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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,986	03/16/2004	Leonard D. Kohn	08-40155-US	3062

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EXAMINER	
LEWIS, AMY A	

ART UNIT	PAPER NUMBER
1613	

MAIL DATE	DELIVERY MODE
11/12/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/801,986	KOHN ET AL.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/20/2009 and 18 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-64 and 69-107* is/are pending in the application.

4a) Of the above claim(s) *70,71,73-81,86,88,92-95,97 and 101-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-64, 69, 72, 82, 85, 87, 89, 90, 91, 96, and 100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the remarks filed 7/20/2009 and 9/18/2009, PROSECUTION IS HEREBY REOPENED. See new and modified rejections set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614

Applicants' arguments, filed 7/20/2009 and 9/18/2009, have been fully considered but they are not deemed to be persuasive to support patentability. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or

objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Rejoinder:

Groups I, II and III from the restriction requirement of 8/28/2006 have been rejoined. Claims 54-64, 69, 72, 82, 85, 87, 89, 90, 91, 96, and 100 are currently under examination, as far as they read upon the elected species of 5-phenyl methylimazole. Claims 70, 71, 73-81, 86, 88, 92-95, 97, and 101-107 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected subject matter, there being no allowable generic or linking claim.

MODIFIED REJECTIONS Double Patenting:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1) Claims 54-64, 69, 72, 82, 85, 87, 89, 90, 91, 96, and 100 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 139-151, 153-179, 187-260 of copending Application No. 11/130922. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application are drawn to the administration of methimazole derivatives and/or cyclic thione derivatives, which encompass 5-phenyl methimazole, for use in the treatment of various autoimmune/inflammatory diseases that encompass those presently claimed. Additionally, the specification at para. [0045] defines the relationship of VCAM and auto-immune-inflammatory disorders, including atherosclerosis.

2) Claims 54-64, 69, 72, 82, 85, 87, 89, 90, 91, 96, and 100 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-33 and 42-44 of U.S. Patent No. 6,365,616 (Kohn et al.), in view of "The Merck Manual".

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent are drawn to administration of methimazole derivatives and/or cyclic thione derivatives, which clearly encompass 5-phenyl methimazole, for use in the treatment of autoimmune diseases.

The Kohn '616 patent does not specifically disclose that lupus/SLE involves cardiovascular complications, however it does state that SLE is characterized by the formation of "a variety or autoantibodies" and "multiple organ system involvement" (see col. 2, lines 58-66).

According to The Merck Manual, noninfective endocarditis is a cardiovascular disease that occurs in a certain population of patients having systemic lupus erythromatosus (SLE).

It would have been obvious to one of ordinary skill in the art at the time the invention was made, that treating a lupus/SLE patient with the claimed compound (5-phenyl methimazole), as taught by Kohn et al., would have also treated cardiovascular disease, such as endocarditis, that was also present in the patient. One would have been motivated to do so by 1) the desire to treat as many symptoms of the disease as possible and 2) having been taught that lupus patients have a scardiovascular complications, as taught by "The Merck Manual".

NEW GROUNDS OF REJECTION:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 54-64, 69, 72, 82, 85, 87, 89, 90, 91, 96, and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kohn et al., U.S. Patent 6,365,616, in view of "The Merck Manual".

Kohn teaches the administration of 5-methyl methimazole to treat autoimmune diseases such as systemic lupus erythromatosus, characterized by a potentially cardiovascular disorder. See column 13 where a particularly preferred subset of methimazole derivatives is described at line 30 where X = S, Y, R^2 in the 3-position, R^1 and R^4 = H and R^2 in the 1-position is methyl. Further, see Table 15, column 49, where 5-phenylmethimazole is, *inter alia*, specifically disclosed.

The inhibition or suppression of cell adhesion, optionally VCAM-1 and/or E-selectin mediated, or IRF-1 dependent VCAM-1 mediated cell adhesion, as well as cytokine-induced cell adhesion, optionally wherein the cytokine is TNF-alpha, are inherent mechanisms of action following the administration of 5-phenyl methimazole.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is

a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

There is no requirement that a person of ordinary skill in the art would have recognized the inherent features at the time of the invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm., Inc., 339 F. 3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2004) ("[T] he fact that a characteristic is a necessary feature or result of a prior art embodiment (that is sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

The Kohn patent does not specifically disclose that lupus/SLE involves cardiovascular complications, however it does state that SLE is characterized by the formation of "a variety or autoantibodies" and "multiple organ system involvement" (see col. 2, lines 58-66).

According to The Merck Manual, noninfective endocarditis is a cardiovascular disease that occurs in a certain population of patients having systemic lupus erythromatosus (SLE).

It would have been obvious to one of ordinary skill in the art at the time the invention was made, that treating a lupus/SLE patient with the claimed compound (5-phenyl methimazole), as taught by Kohn et al., would have also treated cardiovascular disease, such as endocarditis, that was also present in the patient. One would have been motivated to do so by 1) the desire to treat as many symptoms of the disease as possible and 2) having been taught that lupus patients have a scardiovascular complications, as taught by "The Merck Manual".

2) Claims 54-64, 69, 72, 82, 85, 87, 89, 90, 91, 96, and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kohn et al., U.S. Patent 6,365,616, in view of U.S. Patent No. 6924274 (to Lardy and Weeks).

Kohn et al. is applied as above.

Lardy and Weeks list a variety of symptoms and organ systems that are characteristic of lupus, particularly "heart or lung disease, such as an irritation of the heart or lung lining causing pericarditis or pleurisy (occurring in about 30% of persons with lupus)" (see para. [0004]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made, that treating a lupus/SLE patient with the claimed compound (5-phenyl methimazole), as taught by Kohn et al., would have also treated cardiovascular disease that was also present in the patient. One would have been motivated to do so by 1) the desire to treat as many symptoms of the disease as possible and 2) having been taught that lupus patients have a significant occurrence (about 30%) of cardiovascular complications, as taught by Lardy and Weeks.

Claim Rejections - 35 USC § 112

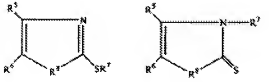
The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1) Claims 54, 55, 57-64, 69, 72, 82, 85, 87, 89, 90, 91 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 54 contains a set of options defining the cyclic thione derivatives, but it is not clear if the groups separated by the ";" are meant to be a mixture or a series of related compounds

wherein the first group is one tautomer and the second and third groups are not tautomers. The portion of claim 54 that is being addressed is copied below:



wherein R^5 is selected from CH_3, CH_2; Ph, H; H, and a phenyl moiety; wherein R^6 is selected from CH_3, CH_2; Ph, H; H, and a phenyl moiety; wherein R^7 is selected from H and CH_3; and R^8 is selected from O, S, NH, and NCH_3.

For example, it is not clear if when defining the groups, it is meant that when R5 is CH3 on the left hand cyclic thione structure, the R5 on the right hand cyclic thione structure must also be a CH3. If this is the case, on the combination where R5 is CH3 on both structures is a tautomer. The other options do not create a tautomeric set. As such, the claim is indefinite and does not clearly define what structures applicant means by this claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 56 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals, such as the methimazole derivatives as defined as tautomers of the structures in claim 54, which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim(s) 56 is inclusive of and directed to

> pharmaceutical composition comprising methimazole derivatives and/or cyclic thione derivatives are selected from the group consisting of tautomeric methimazole derivatives, non-tautomeric methimazole derivatives, and non-tautomeric cyclic thione derivatives, and combinations thereof.

encompass derivatives, ,

which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these additional derivatives meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmacentical Co. Ltd.,* 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the above chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is 571-272-9032. The examiner can normally be reached on Monday-Friday 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amy A Lewis/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614